Inventor Search

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=> FIL MEDLINE CAPLUS BIOSIS WPIDS
FILE 'MEDLINE' ENTERED AT 18:56:34 ON 11 JUN 2002

FILE 'CAPLUS' ENTERED AT 18:56:34 ON 11 JUN 2002
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FILE 'WPIDS' ENTERED AT 18:56:34 ON 11 JUN 2002
COPYRIGHT (C) 2002 THOMSON DERWENT

=> d que l13
L1           808 SEA ("TRYGGVASON K"/AU OR "TRYGGVASON KARL"/AU)
L2            54 SEA ("KALLUNKI P"/AU OR "KALLUNKI PEKKA"/AU)
L3           159 SEA ("PYKE C"/AU OR "PYKE C M"/AU OR "PYKE CHARLES"/AU OR
                 "PYKE CHRISTOPHER"/AU OR "PYKE CHRISTOPHER M"/AU)
L4           970 SEA L1 OR L2 OR L3
L5         35772 SEA LAMININ OR KALININ OR LAMININ (W) 5
L6         17409 SEA GAMMA2 OR GAMMA (W) 2
L7           456 SEA L5 AND L6
L8            47 SEA L4 AND L7
L11      1510077 SEA ANTIBODY
L13           14 SEA L8 AND L11
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8/317,450 10/4/94
800,593 2/18/97
663,147 9/15/00

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L3           159 SEA ("PYKE C"/AU OR "PYKE C M"/AU OR "PYKE CHARLES"/AU OR
                 "PYKE CHRISTOPHER"/AU OR "PYKE CHRISTOPHER M"/AU)
L4           970 SEA L1 OR L2 OR L3
L5         35772 SEA LAMININ OR KALININ OR LAMININ (W) 5
L6         17409 SEA GAMMA2 OR GAMMA (W) 2
L7           456 SEA L5 AND L6
L8            47 SEA L4 AND L7
L9        631622 SEA METASTA? OR INVAS? OR INVAD?
L10           22 SEA L8 AND L9


=> s l10 or l13
L15           25 L10 OR L13

=> dup rem l15
PROCESSING COMPLETED FOR L15
L16           12 DUP REM L15 (13 DUPLICATES REMOVED)

=> d ibib ab 1-12

L16  ANSWER 1 OF 12  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:332666  CAPLUS
DOCUMENT NUMBER:          136:337357
TITLE:                    Laminin chains: diagnostic uses
INVENTOR(S):              Tryggvason, Karl; Kallunki, Pekka;
                          Pyke, Charles
PATENT ASSIGNEE(S):       Finland
SOURCE:                   U.S. Pat. Appl. Publ., 51 pp., Cont.-in-part of U.S.
                          Ser. No. 663,147.
```

CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002052307	A1	20020502	US 2001-756071	20010108
US 5660982	A	19970826	US 1994-317450	19941004
US 6143505	A	20001107	US 1997-800593	19970218

PRIORITY APPLN. INFO.: US 1994-317450 A3 19941004
US 1997-800593 A1 19970218
US 2000-175005P P 20000107
US 2000-663147 A2 20000915

AB The invention concerns the identification, diagnosis, monitoring, and treatment of **invasive** cells using the **laminin 5 gamma-2** chain protein or nucleic acid sequence, or **antibodies** thereto.

L16 ANSWER 2 OF 12 MEDLINE
ACCESSION NUMBER: 2002142250 MEDLINE
DOCUMENT NUMBER: 21850545 PubMed ID: 11860544
TITLE: **Laminin-5 gamma 2** chain as an **invasivity** marker for uni- and multifocal lesions in the lower anogenital tract.
AUTHOR: Nordstrom Britta; Einhorn N; Silfversward C; Sjovall K; **Tryggvason K**; Auer G
CORPORATE SOURCE: Department of Oncology and Pathology, Karolinska Institute and Hospital, S-171 76 Stockholm, Sweden.. Britta.Nordstrom@ks.se
SOURCE: Int J Gynecol Cancer, (2002 Jan-Feb) 12 (1) 105-9. Journal code: 9111626. ISSN: 1048-891X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020307
Last Updated on STN: 20020429
Entered Medline: 20020426

AB During recent decades it has become apparent that there are two types of vulvar disease: the classic type found in elderly women with unicentric and unifocal lesions, and the type found in younger women, in which precancerous and **invasive** changes develop in the anogenital lower tract in a multicentric and multifocal fashion, often over a long period of observation.The **laminin-5 gamma 2** chain is an extracellular protein that is a component of the basement membrane. Recently its expression has been recognized as a marker in cervical cancer that permits identification of **invasive** capacity.The aim of our study was to determine if **laminin-5 gamma 2** chain **antibody** can act as a sensitivity marker of **invasive** capacity in precancerous and **invasive** carcinoma in women with uni- and multifocal changes in the anogenital tract. The result showed that all patients in the older group of women with **invasive** carcinoma of the vulva had moderate to high positive expression of the **laminin-5 gamma 2** chain. In the group of younger patients with multifocal precancerous changes observed over long periods, most of the patients with vulva intraepithelial neoplasia (VIN) 3 showed

laminin-5 gamma 2 chain positivity already in the precancerous changes, and all of them developed **invasivity** during the period of observation. Normal epithelium without atypia was mostly negative or of low immunoreactivity of **laminin-5**. In conclusion, positive **laminin-5 gamma 2** chain expression seems to indicate the **invasiveness** potential of precancerous lesions and is also expressed in all investigated **invasive** carcinomas of the anogenital tract.

L16 ANSWER 3 OF 12 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001517084 MEDLINE
DOCUMENT NUMBER: 21448032 PubMed ID: 11564896
TITLE: **Laminin-5 gamma 2** chain expression correlates with unfavorable prognosis in colon carcinomas.
AUTHOR: Lenander C; Habermann J K; Ost A; Nilsson B; Schimmelpenning H; **Tryggvason K**; Auer G
CORPORATE SOURCE: Department of Surgery, Ersta Hospital, Stockholm, Sweden.. claes.lenander@ersta.se
SOURCE: ANALYTICAL CELLULAR PATHOLOGY, (2001) 22 (4) 201-9. Journal code: 8911016. ISSN: 0921-8912.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20010924
Last Updated on STN: 20020122
Entered Medline: 20011207

AB Expression of the **gamma 2** chain at the **invasive** front of different tumors has indicated an important role for **laminin-5** in cell migration during tumor **invasion** and tissue remodeling. As there is considerable need for reliable **invasion** and prognostic markers we evaluated the correlation of **laminin-5 gamma 2** chain expression with clinicopathologic parameters and patient survival in 93 primary colon carcinomas. Epithelial cells of normal mucosa were consistently negative for staining. In contrast, positive cytoplasmic staining was observed in 89 tumors (96%). Twenty-four (26%) cases were scored as sparse, 34 (37%) as moderate, and 31 (33%) as frequent **gamma 2** chain expression. There was a significant association of **laminin-5 gamma 2** chain expression and local **invasiveness** of colon carcinomas according to Dukes stage (A-C) ($p=0.001$) and tumor budding ($p<0.001$). A statistical significance could also be noted in decreasing tumor differentiation ($p<0.001$) and correlation to tumor size ($p=0.032$). No correlation was observed to tumor site. Univariate analysis identified **laminin-5** ($p=0.010$), tumor differentiation ($p=0.006$) and Dukes grade ($p<0.001$) as significant variables in predicting prognosis. However, by multivariate analyses, this study could not demonstrate that **laminin-5 gamma 2** chain expression is an independent predictive factor for survival.The results indicate that **laminin-5 gamma 2** chain expression is up-regulated during the progression of human colon cancer and that it plays a role in the aggressiveness of these tumors. Demonstration of **laminin-5 gamma 2** chain positivity also facilitates detection of individual cells or minor cell clusters **invading** the surrounding stroma.Figures on http://www.esacp.org/acp/2001/22-4/lenander.htm.

L16 ANSWER 4 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:245379 BIOSIS
DOCUMENT NUMBER: PREV200100245379
TITLE: **Laminin** chains: diagnostic and therapeutic use.
AUTHOR(S): **Tryggvason, Karl (1); Kallunki, Pekka; Pyke, Charles**
CORPORATE SOURCE: (1) Fyysikontic 8, FIN-90570, Oulu Finland
PATENT INFORMATION: US 6143505 November 07, 2000
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Nov. 7, 2000) Vol. 1240, No. 1, pp. No Pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB The instant invention provides for the identification, diagnosis, monitoring, and treatment of **invasive** cells using the **laminin 5 gamma-2** chain protein or nucleic acid sequence, or **antibodies** thereto.

L16 ANSWER 5 OF 12 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2000016413 MEDLINE
DOCUMENT NUMBER: 20016413 PubMed ID: 10547396
TITLE: **Laminin-5** as a marker of **invasiveness** in cervical lesions.
AUTHOR: Skyldberg B; Salo S; Eriksson E; Aspenblad U; Moberger B; **Tryggvason K**; Auer G
CORPORATE SOURCE: Division of Cellular Pathology, Department of Oncology, Karolinska Institute, Stockholm, Sweden..
Barbro.Skyldberg@cck.ki.se
SOURCE: JOURNAL OF THE NATIONAL CANCER INSTITUTE, (1999 Nov 3) 91 (21) 1882-7.
Journal code: 7503089. ISSN: 0027-8874.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991130
AB BACKGROUND: Treatment decisions for cervical cancer, a common disease worldwide, depend on demonstrating whether or not tumor **invasion** of the surrounding tissue has occurred. **Invasion** can be difficult to assess by standard histopathologic methods, especially when limited amounts of tissue are available. Several studies of a variety of cancers have reported increased expression of **laminin-5** -an important attachment protein for epithelial cells-in **invasive** carcinomas. This study was designed to investigate whether the presence of **laminin-5** is related to the **invasive** capacity of cervical lesions. METHODS: We used immunohistochemical methods to stain archival, paraffin-embedded sections of cervical lesions with a polyclonal **antibody** specifically targeting the **gamma2** chain of human **laminin-5** protein. The study sample included 23 lesions of mild and moderate dysplasia (cervical intraepithelial neoplasia [CIN] 1 and 2, respectively), 32 lesions of severe dysplasia or carcinoma in situ (CIN 3), 15 lesions of microinvasive cancer, and 20 lesions of frankly **invasive** cancer. Cellular proliferative activity was also investigated by the use of monoclonal MIB-1 (directed against the antigen Ki-67) and anticyclin A **antibodies**. RESULTS:

Invasiveness of cervical lesions was positively associated with immunohistochemical staining of the **gamma2** chain of **laminin-5** (two-sided P =.001). All CIN 1 and CIN 2 lesions-except one CIN 2 lesion later shown to be **invasive** cancer-and 21 CIN 3 lesions tested negative for the **gamma2** chain of **laminin-5**. Eleven CIN 3 lesions and all **invasive** cancers tested positive for this protein. One lymph node **metastasis** and a pleural **metastasis** from one of the patients with **invasive** cancer showed strong immunohistochemical positivity. Proliferative activity increased with advancement of the lesion but was not confined to cells positive for the **gamma2** chain of **laminin-5**. CONCLUSIONS: These data suggest that **antibodies** directed against the **gamma2** chain of **laminin-5** can identify cervical lesions with **invasive** capacity and thus may be useful as a sensitive marker of early **invasion**.

L16 ANSWER 6 OF 12 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1999370108 MEDLINE
DOCUMENT NUMBER: 99370108 PubMed ID: 10440745
TITLE: Expression of the **laminin gamma2** chain in different histological types of lung carcinoma. A study by immunohistochemistry and in situ hybridization.
AUTHOR: Maatta M; Soini Y; Paakko P; Salo S; **Tryggvason K** ; Autio-Harmainen H
CORPORATE SOURCE: Department of Pathology, University of Oulu, Oulu, Finland.
SOURCE: JOURNAL OF PATHOLOGY, (1999 Aug) 188 (4) 361-8. Journal code: 0204634. ISSN: 0022-3417.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000330
Last Updated on STN: 20000330
Entered Medline: 20000322

AB Sixty-four malignant lung tumours and 12 of their regional lymph node **metastases** were analysed for expression of the **laminin gamma2** chain by immunohistochemistry and in situ hybridization. Expression of the **laminin gamma2** chain was strongest in squamous cell carcinomas, followed by adenocarcinomas and large cell carcinomas. Positive cells, except for large cell carcinomas, were located at the epithelial-stromal interface of tumour clusters. An important exception was small cell lung carcinoma, with only a low level of **laminin gamma2** chain expression. Apart from tumour type, this may reflect the relatively scanty fibrous stroma in these tumours and supports previous observations that small cell lung carcinoma cells, contrary to other types, lack surface expression of alpha(6)beta(4) integrin, the specific **laminin-5** binding receptor. In frozen sections, immunohistochemistry showed linear basement membranes around tumour clusters in squamous cell carcinomas and adenocarcinomas. This shows that carcinoma cells are capable of heavy deposition of the **laminin gamma2** chain around tumour clusters and suggests that a **laminin gamma2** chain-containing substrate may be of significance for the spread and growth of malignant tumours.

L16 ANSWER 7 OF 12 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1999299775 MEDLINE
DOCUMENT NUMBER: 99299775 PubMed ID: 10372560

TITLE: **Laminin-5** promotes adhesion and migration of epithelial cells: identification of a migration-related element in the **gamma2** chain gene (LAMC2) with activity in transgenic mice.
AUTHOR: Salo S; Haakana H; Kontusaari S; Hujanen E; Kallunki T; **Tryggvason K**
CORPORATE SOURCE: Biocenter Oulu and Department of Biochemistry, University of Oulu, Finland.
SOURCE: MATRIX BIOLOGY, (1999 Apr) 18 (2) 197-210.
Journal code: 9432592. ISSN: 0945-053X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990827
Last Updated on STN: 19990827
Entered Medline: 19990819

AB The effects of **laminin-5** and its subunit **gamma2** chain on cell adhesion and migration were studied, and a migration-related cis-acting element was identified in the **gamma2** chain gene (LAMC2) using promoter-reporter gene constructs in transgenic mice. Intact **laminin-5** molecules, but not recombinant **gamma2** chain promoted cell adhesion of human keratinocytes and mouse squamous carcinoma cells, indicating that the **gamma2** chain does not contain a cellular binding site. However, the **gamma2** chain as such is probably involved in the process of cell locomotion, as **antibodies** against the short arm of the chain inhibited migration of carcinoma cells in an in vitro assay. Further evidence for the involvement of the **gamma2** chain in cell migration was obtained by the identification of a cis-acting element in a promoter-lacZ reporter gene construct that was active in migratory epithelial cells of healing wounds in mice made transgenic by microinjection of the construct into fertilized oozytes. The migration active element was located in the sequence between -613 and +55. The same construct, and another one containing 5900 base pairs of the 5' flanking region, yielded very limited expression in cells of normal tissues. The limited expression was, however, only observed in epithelial cells of different tissues, i.e. cell types that normally express **laminin-5** in vivo. The results show that the sequence between -613 and +55 contains elements that can drive expression during epithelial cell migration and that also partially confers more general epithelium expression. However, elements outside -5900 and +55 are needed for normal epithelium expression of the LAMC2 gene.

L16 ANSWER 8 OF 12 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 97247322 MEDLINE
DOCUMENT NUMBER: 97247322 PubMed ID: 9115910
TITLE: Altered distribution and synthesis of **laminin-5** (**kalinin**) in oral lichen planus, epithelial dysplasias and squamous cell carcinomas.
AUTHOR: Kainulainen T; Autio-Harmainen H; Oikarinen A; Salo S; **Tryggvason K**; Salo T
CORPORATE SOURCE: Oral and Maxillofacial Department, Oulu University Hospital, Finland.
SOURCE: BRITISH JOURNAL OF DERMATOLOGY, (1997 Mar) 136 (3) 331-6.
Journal code: 0004041. ISSN: 0007-0963.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970506
Last Updated on STN: 19970506
Entered Medline: 19970422

AB **Laminin-5** is a glycoprotein which mediates epithelial cell adhesion to the basement membrane. This study describes the distribution and synthesis of **laminin-5** in oral lichen planus, epithelial dysplasias, squamous cell carcinomas and a lymph node **metastasis** using immunohistochemistry and in situ hybridization. In normal oral mucosa and lichen planus, immunoreaction to the **laminin-5** was seen as a thin continuous, delicate line in the basement membrane region, although slight irregularities in the thickness and intensity of the immunoreaction could be detected in some cases with lichen planus. In epithelial dysplasias, the **laminin-5** staining was discontinuous and more diffuse compared to lichen planus and normal mucosa. The immunoreaction was generally extracellular, although in some cases with lichen planus and epithelial dysplasia there were a few basal epithelial cells showing cytoplasmic staining. The **invasive** carcinomas and the lymph node **metastasis** showed a striking, intense cytoplasmic, staining of the carcinoma cells along the **invasive** border of the neoplastic islands and in individual infiltrating carcinoma cells. Using in situ hybridization, the **laminin-5 gamma 2** chain mRNA expression could not be detected in normal oral mucosa whereas, in non-dysplastic lichen planus and, more strongly, in dysplasias, there was a clear increase in the expression of **laminin-5** mRNA in the basal epithelial cells. The most intensive signal was detected in the **invasive** front of the oral squamous cell carcinomas and the lymph node **metastasis**. We conclude that, in oral squamous cell carcinoma, there is altered synthesis and secretion of **laminin-5** mRNA and protein. It is also evident that in dysplastic lesions of oral epithelium the synthesis and distribution of **laminin-5** is abnormal.

L16 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 6
ACCESSION NUMBER: 1996:377252 CAPLUS
DOCUMENT NUMBER: 125:49293
TITLE: Human **laminin 5 .gamma.** **2**-chain **antibody** for diagnosis and antisense oligonucleotides for inhibition of malignant cell **invasive** growth
INVENTOR(S): **Tryggvason, Karl; Kallunki, Pekka; Pyke, Charles**
PATENT ASSIGNEE(S): Finland
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9610646	A1	19960411	WO 1995-EP3918	19951004

W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT,

LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 5660982	A	19970826	US 1994-317450	19941004
CA 2201865	AA	19960411	CA 1995-2201865	19951004
AU 9537451	A1	19960426	AU 1995-37451	19951004
AU 699183	B2	19981126		
EP 784703	A1	19970723	EP 1995-935428	19951004
EP 784703	B1	19990714		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 182180	E	19990715	AT 1995-935428	19951004
ES 2133813	T3	19990916	ES 1995-935428	19951004

PRIORITY APPLN. INFO.: US 1994-317450 A 19941004
WO 1995-EP3918 W 19951004

AB The instant invention provides for the identification, diagnosis, monitoring, and treatment of malignant **invasive** cells using the **laminin 5 .gamma.-2** chain protein or nucleic acid sequence, and **antibodies** or antisense oligonucleotides.

L16 ANSWER 10 OF 12 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 97117923 MEDLINE
DOCUMENT NUMBER: 97117923 PubMed ID: 8958807
TITLE: Expression of the **laminin gamma 2** chain in pancreatic adenocarcinoma.
AUTHOR: Soini Y; Maatta M; Salo S; **Tryggvason K**; Autio-Harmainen H
CORPORATE SOURCE: Department of Pathology, University of Oulu, Sweden.
SOURCE: JOURNAL OF PATHOLOGY, (1996 Nov) 180 (3) 290-4. Journal code: 0204634. ISSN: 0022-3417.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19970106

AB Forty-two pancreatic adenocarcinomas were investigated immunohistochemically and by in situ hybridization for the expression of the **laminin gamma 2** chain. In 41 cases, intracytoplasmic immunoreactivity for the **gamma 2** chain was seen. Positive tumour cells were located especially at the epithelial-stromal interface of the tumour cell islands. In 22 cases, diffuse **laminin gamma 2** chain immunoreactivity could also be seen in stroma and in seven cases, occasional positivity was detected in the neoplastic basement membranes. Signals for **laminin gamma 2** chain mRNA in tumour cells displayed a distribution similar to that observed on immunohistochemistry. There were significantly more cases with less than 20 per cent of **laminin gamma 2** chain-positive tumour cells in tumours extending to peripancreatic tissues and/or tumours with regional or distant **metastases** ($p = 0.029$). A corresponding statistical significance could also be noted in the mRNA level ($P = 0.025$). The results show that pancreatic adenocarcinomas display a high activity of **laminin gamma 2** chain synthesis. Tumours with a strong **laminin gamma 2** chain synthesis show a lower **invasive** and **metastatic** potential than tumours with a weak or moderate **laminin gamma 2** chain expression.

L16 ANSWER 11 OF 12 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 95393419 MEDLINE
DOCUMENT NUMBER: 95393419 PubMed ID: 7664291
TITLE: **Laminin-5** is a marker of **invading** cancer cells in some human carcinomas and is coexpressed with the receptor for urokinase plasminogen activator in budding cancer cells in colon adenocarcinomas.
AUTHOR: **Pyke C**; Salo S; Ralfkiaer E; Romer J; Dano K; **Tryggvason K**
CORPORATE SOURCE: Finsen Laboratory, Rigshospitalet, Copenhagen, Denmark.
SOURCE: CANCER RESEARCH, (1995 Sep 15) 55 (18) 4132-9.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199510
ENTRY DATE: Entered STN: 19951020
Last Updated on STN: 19951020
Entered Medline: 19951006

AB Recombinant human **gamma 2** chain of **laminin-5** was expressed in Escherichia coli, and used to generate specific polyclonal **antibodies** which were used to study the distribution of the protein in human cancers. A total of 72 biopsies of human cancers were stained, including 23 cases of colon adenocarcinomas, 16 ductal breast carcinomas, 9 malignant melanomas, 14 squamous cell carcinomas of the skin and cervix, and 10 sarcomas. As a control for the specificity of the **antibodies**, we performed in situ hybridization on adjacent sections of a number of the cases, and in all of these cases the localization of the **gamma 2** chain protein and mRNA was identical. We found **gamma 2** chain immunoreactivity in cancer cells in all cases of colon adenocarcinomas and squamous cell carcinomas but not in any of the sarcomas, supporting the view that the **laminin-5** protein is specific for cells of epithelial origin. Notably, in all of the cases of colon adenocarcinomas, the positive staining was invariably associated with budding cancer cells located at the tip of **invading** malignant epithelium, whereas the cancer cells deeper in the tumors were most often negative. The staining was cytoplasmic in all cases and only in one case did we see additional extracellular immunoreactivity, indicating that this **laminin** isoform in cancer tissue is not laid down in the extracellular matrix but probably exerts its function at the cell surface or in its immediate vicinity. Using in situ hybridization to analyze the coexpression of **laminin-5** and components of the plasminogen activation system, we found that the histological distribution of **laminin-5**-positive budding cancer cells at the **invasion** front in colon adenocarcinomas was identical to that of the receptor for urokinase-type plasminogen activator. These findings suggest that **laminin-5** is a marker of **invading** cancer cells in at least some human malignancies, and that it therefore might represent a valuable marker for the **invasive** potential of these cancers. The colocalization of **laminin-5** and urokinase-type plasminogen activator receptor in a subset of cancer cells in colon cancer also suggests that a controlled up-regulation of a number of gene products is a characteristic of budding colon cancer cells, and that these gene products serve functions crucial for the **invasive** phenotype of these cancer cells.

L16 ANSWER 12 OF 12 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 95029709 MEDLINE

DOCUMENT NUMBER: 95029709 PubMed ID: 7943170
TITLE: The **gamma 2** chain of **kalinin/laminin 5** is preferentially expressed in **invading** malignant cells in human cancers.
AUTHOR: **Pyke C**; Romer J; **Kallunki P**; Lund L R; Ralfkiaer E; Dano K; **Tryggvason K**
CORPORATE SOURCE: Finsen Laboratory, Rigshospitalet, Copenhagen, Denmark.
SOURCE: AMERICAN JOURNAL OF PATHOLOGY, (1994 Oct) 145 (4) 782-91. Journal code: 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199411
ENTRY DATE: Entered STN: 19941222
Last Updated on STN: 19941222
Entered Medline: 19941107

AB All known **laminin** isoforms are cross-shaped heterotrimeric molecules, consisting of one heavy alpha chain and two light beta and gamma chains. Recently, a cDNA encoding a new gamma chain from **laminin 5** (also known as **kalinin**) was sequenced. This chain, named **gamma 2**, showed extended homology to the classical gamma 1 chain but differed from this by lacking the terminal globular domain. Recent data, indicating an important role of the **gamma 2** chain gene in establishing adhesion contacts between epithelial cells and basement membranes, prompted us to investigate whether the **gamma 2** chain gene is aberrantly expressed in cancer tissue, and if so whether its localization could provide clues to its possible role in cancer dissemination. Routinely processed tissue specimens from 36 cases of human cancer were investigated, including 16 cases of colon adenocarcinoma, 7 ductal mammary carcinomas, 4 squamous cell carcinomas, 3 malignant melanomas and 6 sarcomas. In situ hybridization for the detection of mRNAs for the **gamma 2** chain and for the classical **laminin** chains alpha 1, beta 1, and gamma 1 was performed using S-35 labeled antisense RNA probes. As positive control of the specificity of the **gamma 2** chain mRNA detection, two different anti-sense probes derived from two nonoverlapping cDNA clones were used. Malignant cells were found to express the **gamma 2** chain in 29 of the 30 carcinomas studied and the expression was particularly high in cancer cells located at the **invasion** front. In contrast, mesenchymally derived cancer cells in three different types of sarcomas did not express the **gamma 2** chain. In colon cancer there was a clear histological correlation between the expression of **gamma 2** chain by cancer cells and their engagement in tumor budding processes. **Laminin** chains alpha 1, beta 1, and gamma 1 were weakly expressed throughout cancerous areas with no apparent correlation to sites of **invasion**. The aberrant expression of the **gamma 2** chain gene seen in **invasively** growing cancer cells point to a role of this molecule in establishing focal adhesions of cancer cells to the extracellular matrix during their migration through surrounding normal tissue.